A

```
Human  MSAGDAVCTGWLVKSPPERKLQRYAWRKRWFVLRRGRMSGNPDVLEYYRNKHSSKPIRVI 60
Murine MSTGDTVCMGWLIKSPPERKLQRYAWRKRWFVLRRGRMSGNPDVLEYYRNKHSNKPIRVI 60
       **:**:** ***:*********************************** ****.
```
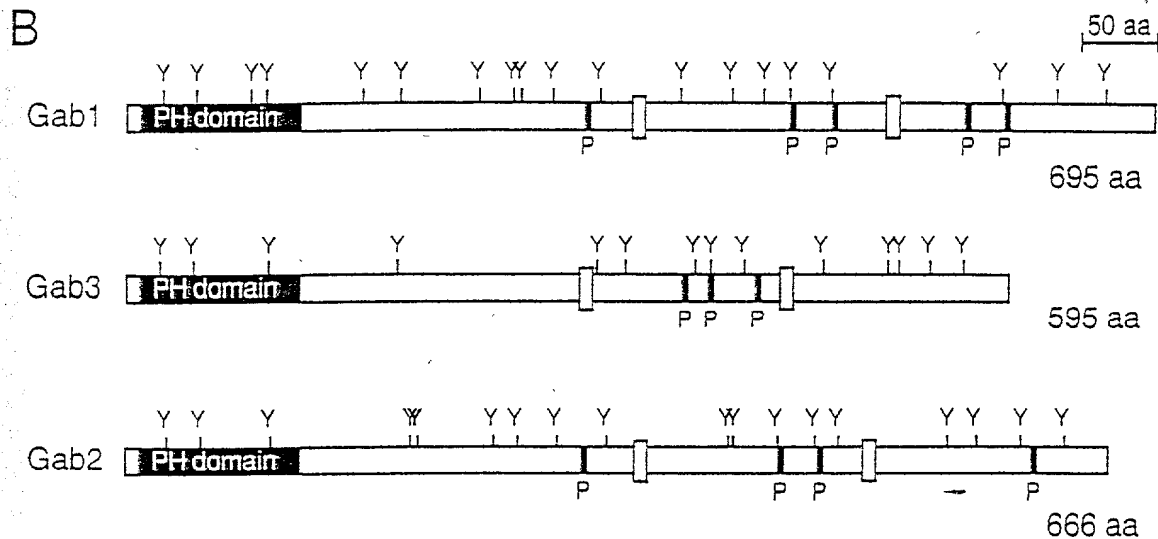
```
Human  DLSECAVWKHVGPSFVRKEFQNNFVFIVKTTSRTFYLVAKTEQEMQVWVHSISQVCNLGH 120
Murine DLSECTVWKHAGPGFIRKEFQKNFVFIVKTTSRTFYLVAKTEEEMQVWVHSISQVCNFSH 120
       *****:****.** *:*****:*********************:************::.*
```

```
Human  LEDGADSMESLSYTPSSLQPSSASSLLTAHAASSSLPRDDPNTNAVATEETRSESELLFL 180
Murine LEDGADSMESLSHMPSSFQPSPASSLHTVHVANSALLKDDGNTNSVVTEETRRESEFLFL 180
       ************: ***:***.**** *.*.*.*:* :** ***.*.***** ***.***
```

```
Human  PDYLVLSNCETGRLHHTSLPTRCDSWSNSDRSLEQASFDDVFVDCLQPLPSSHLVHPSCH 240
Murine PDYLILSNCETGRLHHASLPTRCDSWSNSNHSLAQTSFDDVFLDGLQPFISNNLVHPLHH 240
       ****:.**********:***********::** *:******.* ***: * .:****  *
```

```
Human  GSGAQEVPSSRPQAALIWSREINGPPRDHLSSSPLLESSLSSTIQVDKNQGSLPCGAKEL 300
Murine GKVSQDFPSIRPQASLIWNREINGPSRNLMSSSPLLESSLNPTVHVEEKQVSLPSGVKEL 300
       *. :*:.** ****:***.****** .*: :**********..:*::::* ***.*.***
```

```
Human  DIMSNT PPPRPPKP SHLSERRQEE--WSTHSGSKKPECTLVPRRISLSGLDNMRTWKADV 358
Murine NIMSNI PPPRPPKP SYLSEQRQDQPLLTGHSSNKKPGYTMVPRRISLSGLDHVGSWKGDV 360
       :**** ********* :***:**::   : **..*** *:*************:: :**.**
```

```
                                             p85?                          p85?
Human  EGQSLRHRDKRLSLNLPCRFS PMYP TASASIEDSYV PMSP QAGASGLGPHCSPDDYIPMN 418
Murine QSQSLRHRDKRLSLNLPCKFS PIYP TASPSAEDSYV PMSP KGTASELRPHCSQDDYIPMS 420
       :.*************:*** .***:*** .* ********:. ** * **** ******.
```

```
Human  SGSISSPL PELP ANLE PPPVNRDLKP QRKSRPPPLDLRNLSIIREHASLTRTRTVPCSRT 478
Murine S----SML PELP ADLE PPPVNRNLKP QRKSRPPPLDSRNLSTIQEHTSLTRTYTVPCNRT 476
       *     * *****:*******:********** **** *:**:***** ****.**
```

```
                                         p85?
Human  SFLSPERNGINSARFFANPVSREDEES-----------YIEMEEHRTASSLSSGALTWTK 527
Murine SFLSPQRNGINCARLFSTPSEEEEEEEEEEEEEEEEKYIQMEEYGTVSSLSRSALSWTK 536
       ****:*****.**:*..* ..*:**.        **:***: *.**** .**:***
```

```
          SHP2                            SHP2
Human  KFSLDYLALDFNSASPAPMQQKLLLSEEQRVDYVQVDEQKTQALQSTKQEWTDERQSKV 586
Murine KFSLDYLALDFNSTSPAPVQKKLLLSEEQRVDYVQVDEQKTQAFRSTKQAWTDERQSKV 595
       *************:****:*:*******************************:**** ********
```

Figure 1A

B

Gab1 PH domain ... Y Y YY Y Y Y YY Y Y Y Y Y Y Y Y Y
       P   P P   P P
       695 aa

Gab3 PH domain ... Y Y Y Y YY Y Y Y YY Y Y
                    P P P
       595 aa

Gab2 PH domain ... Y Y YY Y Y Y Y YY Y Y Y Y Y Y
                 P   P P   P
       666 aa

50 aa

C

```
Gab3  MSTG--D-TVCMGWLIKSPPERKLQRYAWRKRWFVLRRGR      37
Gab2  MSGGGGDDVVCTGWLRKSPPEKKLRRYAWKKRWFILRSGR      40
Gab1  MSGG--E-VVCSGWLRKSPPEKKLKRYAWKRRWFVLRSGR      37
      ** *   : .** *** ****:.**:****::***.** **

Gab3  MSGNPDVLEYYRNKHSNKPIRVIDLSECTVWKHAGPGFIR      77
Gab2  MSGDPDVLEYYKNEHSKKPLRIINLNLCEQVD-AGLTFNK      79
Gab1  LTGDPDVLEYYKNDHAKKPIRIIDLNLCQQVD-AGLTFNK      76
      ::*:*******:*.*::**:*:*:*.  *    .  ** .* :

Gab3  KEFQKNFVFIVKTTSRTFYLVAKTEEEMQVWVHSISQVCN     117
Gab2  KELQDSFVFDIKTSERTFYLVAETEADMNKWVQSICQICG     119
Gab1  KEFENSYIFDINTIDRIFYLVADSEEDMNKWVRCICDICG     116
      **::...::*  ::*  .*  ****.:*  :*: **:.*.::*.
```

Figure 1B and C